

An age-structured continuum model for myxobacteria

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Abstract

Myxobacteria are social bacteria, that can glide in 2D and form counter-propagating, interacting waves. Here we present a novel age-structured, continuous macroscopic model for the movement of myxobacteria. The derivation is based on microscopic interaction rules that can be formulated as a particle-based model and set within the SOH (Self-Organized Hydrodynamics) framework. The strength of this combined approach is that microscopic knowledge or data can be incorporated easily into the particle model, whilst the continuous model allows for easy numerical analysis of the different effects. This allows to analyze the influence of a refractory (insensitivity) period following a reversal of movement. Our analysis reveals that the refractory period is not necessary for wave formation, but essential to wave synchronization, indicating separate molecular mechanisms.

Key words: Self-propelled particles, nematic alignment, hydrodynamic limit, generalized collision invariant, diffusion correction, myxobacteria, wave formation, refractory period.

AMS Subject classification: 35L60, 35K55, 35Q70, 82C05, 82C22, 82C70, 92D50

1 Introduction

Myxobacteria are a fascinating example for how simple cell-cell interaction rules can lead to emergent, collective behavior. These single-celled organisms have the ability to move on two dimensional surfaces and form large colonies. When *swarming*, the colony exists as a rather uniform mono- or multi-layer of densely packed cells with single cells occasionally venturing away from the main swarm body. Myxobacterial swarms are predatory, searching and killing prey as a collective, which is one reason why these bacteria have often been called *social* bacteria [24]. Upon meeting prey, but also under starvation conditions the cells enter a *ripple phase*, during which periodic density waves are formed [52]. When two waves traveling in opposite directions collide, the waves appear to pass through each other unaffectedly. However, by tracking individual bacteria [50, 57] it was discovered that most cells in the wave crests in fact reverse their direction of movement, showing that the density waves are actually being reflected off each other. Myxobacteria reverse without turning, by internally exchanging the lagging and the leading pole. Isolated bacteria reverse spontaneously (on average every 10 min), however, their reversal rate increases as a response to higher densities of other bacteria around them. Although the precise function of rippling is not known, it often serves as a prelude and also overlaps with an *aggregation phase*: in this developmental stage bacteria aggregate into several growing mounds which eventually rise out of the plane and form large three dimensional fruiting bodies. Both waves and aggregates are macroscopic structures with typical length scales of 100 μm , whereas individual bacteria are only a few microns long. Biologically this makes myxobacteria an interesting and suitable research object for understanding the development of multicellular cooperation, the basis of all complex life forms. Finally, the myxobacteria's unique metabolites have also rendered them an attractive source for potential new drugs [58, 49].

Myxobacteria are rod shaped and have the ability to glide on surfaces, leaving behind a slime trail. Both the genetical basis for their movement and the physical mechanism of force creation is still not well understood. Already in the 1970s Hodgkin and Kaiser [30] discovered that *M. xanthus* uses two separate motility systems: A-motility (for adventurous) that allows single cells to move individually, and S-motility (for social), which enables cells to move in a collective. The latter utilizes type IV pili to attach to neighboring cells. A-motility is much less understood and the models that have been brought forward include propulsion by slime excretion [59], force creation by focal adhesions [42] and, most recently, the *helical rotor model*, which proposed propulsion by motor proteins moving on helical cytoskeletal fibers. [45, 41, 59] provide an overview of these models and open questions.

The various social and cooperative behavior in observed myxobacterial colonies raises questions about the mechanisms of cell-cell communication. The most important mechanism responsible for inducing both ripple formation and aggregation has been found to be C-signaling: The C-factor is a 17-kD protein associated with the cell surface. It has been shown that direct cell-cell contact is necessary for C-signaling and that the exchange is facilitated via end-to-end contacts [35, 33]. Isolated cells exposed to purified C-factor

show an increase in reversal frequency [50], suggesting that cell-to-cell contacts increase the probability for a cell to reverse.

In this work we try to shed light on some of the questions associated with ripple formation: What primary effect of C-signaling causes a uniformly spread swarm to start forming ripples? Are density-dependent changes in reversal frequency enough to explain the formation of opposing, periodic wave trains? One idea brought forward in [31] and inspired by *D. discoideum* is that of an insensitivity or refractory period. Based on the observation that there seems to be a minimum time of around 40 sec [57] between two reversals of the same bacterium, it is suggested that bacteria become insensitive to C-signaling immediately after they have reversed. Using mathematical modeling we show that a refractory period is not necessary for the formation of traveling bands as such, but rather for controlling the width of the waves as well as their wavelength. By analyzing the composition of waves in terms of insensitive and sensitive cells, we discover a possible mechanism how periodic waves are created and maintained in myxobacterial colonies.

While mutation experiments provide valuable insight, computational models offer a powerful alternative to test and analyze different mechanistic biological models. Detailed measurements and statistics about single cell behavior [50, 57] as well as mutation experiments provide the quantitative data necessary to formulate, parametrize and validate mathematical models. In many cases when modeling biological or physical systems one of the first modeling decisions is whether to use an individual- or particle-based model (IBM), in which the individual agents (in our case bacteria) interact by simple rules or to use a continuum model, in which the evolution of macroscopic quantities such as densities or mean directions are described by differential equations [40]. Advantages of IBMs are that they generally allow for an easy incorporation of biological knowledge or hypotheses and can deal with noise in a straightforward way. However the analysis of the model is often limited to running a large number of simulations and little mechanistic insight is gained. For (macroscopic) differential equations on the other hand a large analytical toolbox ranging from asymptotic methods to linear stability analysis and bifurcation theory is available, which can produce precise results about the parameter dependence of solution behavior, etc. However for biological systems it is often difficult to derive continuous models, in many cases ad hoc models are used in which some desired system behavior is already built into the derivation, thereby limiting the explanatory potential of the model.

The derivation of macroscopic models from IBMs of collective dynamics has been the subject of an intense literature with a particular focus on applications to biology. This derivation proceeds through an intermediate modelling level called the kinetic or mean-field model [3, 4, 5, 8]. The derivation from kinetic to macroscopic models of collective dynamics faces the problem of the lack of conservation relations (such as the lack of momentum conservation, see e.g. the review [56]). A recent breakthrough is the so-called generalized collision invariant concept [21, 23, 26] subsequently developed in a variety of biological contexts (sperm dynamics [13], tissue self-organization [14], flocking [16, 17]) as well as physical (micromagnetism [18]) or social (economics [19]) contexts. Other models of collective dynamics can be found in [1, 2, 9, 10, 11, 12, 25, 27, 39, 43, 46, 48, 54]. In

this paper, to model the refractory period between two reversals of myxobacteria, we use the concept of a local time that is reset to zero after each reversal. This idea is borrowed from similar ideas used in neuron dynamics (see e.g. [47]) itself being a variant of the renewal equation used to model the cell cycle [29].

2 Model Presentation

We present a model hierarchy at the individual and macroscopic levels. We start with an individual-based model (Sec. 2.1) describing the position and velocity of each bacterium as well as its internal biochemical age variable, which can be interpreted as memory of the bacterium. Here *age* refers to the time passed since the last reversal. From there we systematically derive an age-structured continuous model for the macroscopic quantities, density and nematic mean direction (Sec. 2.2) where the age variable is still continuous. As a last step we discretize the age variable and assume only two groups or ages: being in the refractory period (i.e. being insensitive to C-signaling) or being sensitive to C-signaling. This results in a macroscopic 2-age model (Sec. 2.3), that forms the basis of the subsequent analysis.

Model Assumptions. Fig. 1 shows the main model ingredients and assumptions:

M1: Bacteria move in 2D with constant speed, in the direction of their orientation. This orientation is subject to random noise (Fig. 1.B).

M2: Bacteria align nematically with other bacteria within their immediate vicinity (Fig. 1.A).

M3: Bacteria can reverse their orientation. Their reversal rate is a function of the local density of opposing bacteria (Fig. 1.C1/C3).

M4: After a reversal, bacteria go through a refractory period of fixed length, denoted by T , during which they cannot reverse (Fig. 1.D/C2).

M2 can be interpreted as the effect of physical interactions between hard rods and models size exclusion effects and steric interactions. **M3** is a consequence of the contact-dependence of C-signaling, which we assume to act only over very short distances.

2.1 The Individual Based Model (IBM)

We describe the movement of N individual myxobacteria. For $i \in \mathcal{N} := \{1, \dots, N\}$, the i -th bacterium at time $t > 0$ is characterized by its center of mass $X_i(t) \in \mathbb{R}^2$, its orientation angle $\Theta_i(t) \in [-\pi, \pi)$ (defined modulo 2π) and an age variable $s_i(t) \geq 0$, related to the time since the bacterium's last reversal.

Movement and Alignment. Bacteria move with constant speed $v_0 > 0$ in the direction $v(\Theta_i(t)) := (\cos \Theta_i(t), \sin \Theta_i(t))^T$. To model nematic alignment, we follow [20] and assume that the following stochastic differential equations govern the evolution of $X_i(t)$ and $\Theta_i(t)$:

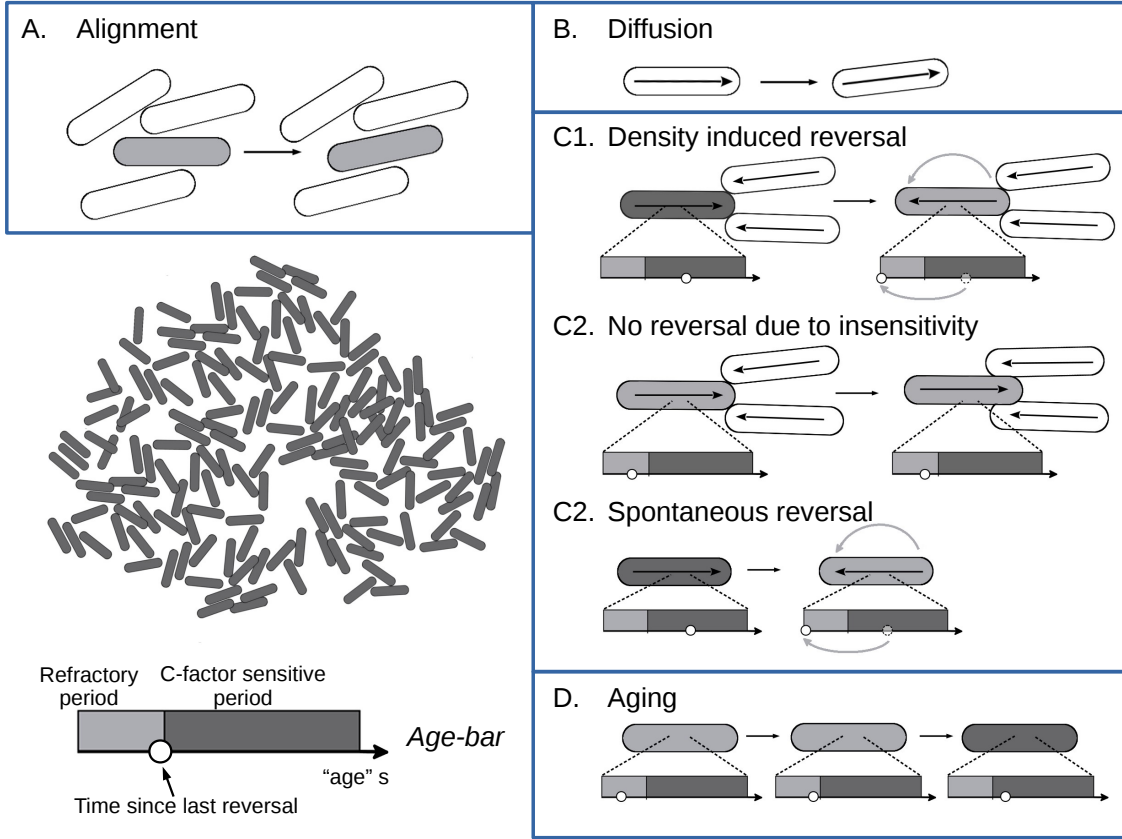


Figure 1: *Ingredients of the memory-dependent myxobacteria model.* A: Nematic Alignment. The bacterium depicted in gray aligns nematically with its neighbors due to steric interactions and size exclusion effects. B: Angular Noise. The bacterium's orientation is subject to random fluctuation. C/D: Reversals and Aging. Bacteria can either be insensitive to C-signaling (light gray) or sensitive (dark grey). The age bar (explained in the lower, left corner) depicts the two periods and the bacterium's current state (white dot). Upon meeting oppositely moving bacteria, a bacterium can reverse, if sensitive to C-signaling (C1) or not, if in the refractory period (C2). They can also reverse spontaneously (C3). Insensitive bacteria age into a sensitive state (D) and reversals reset their age variable to zero (C1 and C3).

$$\begin{cases} \frac{dX_i}{dt} = v_0 v(\Theta_i(t)), & (2.1a) \\ d\Theta_i = -\nu \text{Sign}(\cos(\Theta_i - \bar{\Theta}_i)) \sin(\Theta_i - \bar{\Theta}_i) dt - 4D \cos(\Theta_i - \bar{\Theta}_i) \sin(\Theta_i - \bar{\Theta}_i) dt \\ \quad + \sqrt{2D \cos^2(\Theta_i - \bar{\Theta}_i)} dB_t^i. & (2.1b) \end{cases}$$

Remark 2.1 Note that the term $4D \cos(\Theta_i - \bar{\Theta}_i) \sin(\Theta_i - \bar{\Theta}_i) dt$ presents a subtle difference to the model presented in [20] and arises from a different interpretation of the stochastic

differential equations (SDEs): Using the usual Ito convention, this term is necessary to be consistent with both the numerical implementation presented below and the Fokker-Planck equation derived in the App. A.1. In [20] the SDEs were interpreted in the Backward Ito sense (also called isothermal convention [36, 37, 38]), and hence formulated without this term.

The parameter $\nu > 0$ measures the alignment frequency to the local mean direction $\bar{\Theta}_i$. Bacteria either align with it (if $\cos(\Theta_i - \bar{\Theta}_i) > 0$) or against it (if $\cos(\Theta_i - \bar{\Theta}_i) < 0$). The nematic mean direction $\bar{\Theta}_i$ can be understood as an average of lines going through each bacterium. It is defined by

$$\begin{pmatrix} \cos(2\bar{\Theta}_i) \\ \sin(2\bar{\Theta}_i) \end{pmatrix} = \frac{J_i}{|J_i|} \quad \text{with} \quad J_i = \sum_{k: |X_k - X_i| \leq R} \begin{pmatrix} \cos(2\Theta_k) \\ \sin(2\Theta_k) \end{pmatrix}.$$

J_i represents the nematic mean current and the parameter $R > 0$ specifies the interaction range of the alignment. $\bar{\Theta}_i$ has to be understood modulo π and we always choose $\bar{\Theta}_i \in [0, \pi)$. A more detailed discussion can be found in [20]. The angular noise is modeled by the stochastic process dB_t^i , describing independent Brownian motion of intensity $D \cos^2(\Theta_i - \bar{\Theta}_i)$, where $D > 0$. The term $\cos^2(\Theta_i - \bar{\Theta}_i)$ aids the separation into two groups of bacteria traveling in opposite direction and is described in detail in [20]. This concludes the modeling of assumptions **M1** and **M2**.

Reversals and Insensitivity. To model assumptions **M3** and **M4** we start by noting that bacteria can reverse their orientation, which changes Θ_i to $\Theta_i + \pi$. The reversal frequency depends on physical contact during which the signaling molecule C-factor is exchanged. We assume that immediately after a reversal, bacteria go through a refractory period of length T , during which they are insensitive to C-signaling. We therefore endow each bacterium with an *age* variable $s_i(t) > 0$ which measures the time elapsed since its last reversal, normalized by the refractory period T :

$$s_i(t) = \frac{t - \tau_i}{T},$$

where τ_i records the time of the last reversal for the i -th particle. The dynamics of s_i are given by

$$\begin{cases} \frac{ds_i}{dt} = \frac{1}{T}, & \text{if } t > \tau_i \text{ and } t \text{ is not a reversal time,} \\ s_i = 0, & \text{if } t \text{ is a reversal time.} \end{cases}$$

We model C-signaling sensitivity by a step function $\phi(s) \in \{0, 1\}$:

$$\phi(s) = \begin{cases} 0, & \text{if } 0 \leq s \leq 1 \text{ (refractory period),} \\ 1, & \text{if } s > 1 \text{ (C-factor sensitive period).} \end{cases}$$

To model **M3**, we assume that an individual bacterium's reversal rate is a function of the local density of bacteria oriented opposite to it. To that end, we define the local densities ρ_{\pm}^i in the i -th bacterium's neighborhood $\mathcal{B}_i(X) = \{X : |X - X_i| \leq R\}$ as

$$\rho_{\pm}^i = \frac{1}{|\mathcal{B}_i|} \text{Card}\{k \in \mathcal{N} \mid X_k \in \mathcal{B}_i \text{ and } \pm \cos(\Theta_k - \bar{\Theta}_i) \geq 0\},$$

where ‘Card’ is the cardinal of a set and $|\mathcal{B}_i|$ the area of \mathcal{B}_i . Since both are related to physical contact, we choose the interaction radii of density sensing and alignment to be equal, however in general they could be different. The subscripts \pm indicate whether the density refers to bacteria moving with (+) or against (−) the i -th particle. The reversal frequency as a function of density of opposing bacteria is denoted by $\lambda(\rho)$. Since higher concentration of opposing bacteria have been observed to cause more frequent reversals, we assume $\lambda(\rho)$ to be an increasing function of ρ . More discussion is provided in Sec. 2.4.

The total reversal function $\Lambda(\rho, s)$ takes into account both of the above factors, namely the density and the refractory period, and is defined by

$$\Lambda(\rho, s) = \lambda(\rho)\phi(s). \quad (2.2)$$

Finally, the probability that the i -th particle reverses at $t + \Delta t$ is modeled as a Poisson process:

$$\begin{aligned} & \Pr\{\Theta_i(t + \Delta t) = \Theta_i(t) + \pi | \Theta_i(t + \tau) = \Theta_i(t) \quad \forall \tau \in [0, \Delta t]\} \\ &= 1 - \exp\left(-\Lambda(\rho_{-\text{Sign} \cos(\Theta_i - \bar{\Theta}_i)}, s_i(t))\Delta t\right). \end{aligned}$$

This completes the description of the Individual Based Model (IBM). Numerical results are presented in Sec. 3.1.

2.2 The Macroscopic Continuous-Age Model

The IBM presented in Sec. 2.1 consists of $4N$ coupled stochastic differential equations for typical bacterial colony sizes of $N \approx 10^6$. We therefore derive a macroscopic model that consists of only three partial differential equations. The derivation strategy uses the *Self-Organized Hydrodynamics* (SOH) framework, which allows a systematic derivation of hydrodynamic equations for particle systems that do not have enough conserved quantities, a common obstacle in biological systems. The derivation follows [20] and is described in more detail in App. A.1; however its structure can be summarized as follows. First a mean field model is derived, which leads to a Fokker-Planck equation for the 1-particle distribution function. A hydrodynamic scaling introduces a small parameter representing the difference in microscopic and macroscopic time and spatial scales. Taking this parameter to zero, one finds that the equilibrium distribution function is locally characterized by three quantities: The nematic mean direction $\bar{\theta}$, the density of particles aligned with it, ρ_+ and that of particles anti-aligned with it, ρ_- . The macroscopic model describes how these three quantities change in time and space and how the densities depend on the bacteria’s biochemical age.

The macroscopic continuous-age model. We denote the spatial variable by $x \in \mathbb{R}^2$, the age variable by $s \in [0, \infty)$ and time by $t > 0$. Then $\bar{\theta}(x, t) \in [0, \pi)$ describes the local nematic mean direction, which is independent of s . We recall that $v(\bar{\theta}) := (\cos(\bar{\theta}), \sin(\bar{\theta}))^T$ and define v^\perp as its left-oriented orthogonal. We denote by $\rho_+(x, s, t)$ and $\rho_-(x, s, t)$ the local densities of bacteria of age s that are transported in the directions $v(\bar{\theta})$ and $-v(\bar{\theta})$

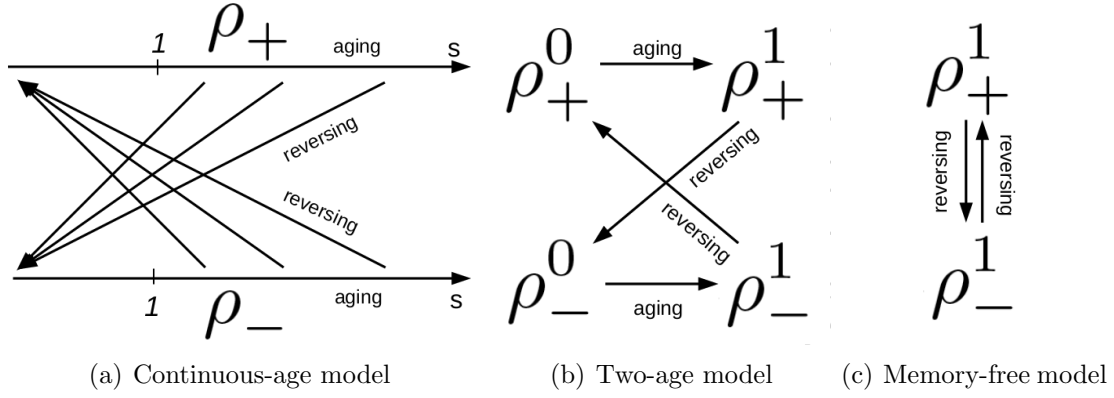


Figure 2: Reaction terms in the three macroscopic models: In the continuous-age model, (a) the densities ρ_{\pm} depend on the continuous age variable s . Particles can *age* along s (horizontal arrows) or reverse, if $s > 1$ (diagonal arrows), which lets them join the other group at age $s = 0$. In the 2-age model (b), there are only 2 age groups, insensitive to C-signaling or sensitive to C-signaling, denoted by the superscripts 0 and 1. In the memory-free model (c), all particles are sensitive to C-signaling and there is no aging.

respectively. $\bar{\theta}(x, t)$, $\rho_{\pm}(x, s, t)$ fulfill the following system of equations:

$$\partial_t \rho_+ + d_1 v_0 \nabla_x \cdot (\rho_+ v(\bar{\theta})) + \frac{1}{T} \partial_s \rho_+ = -\Lambda(\sigma_-, s) \rho_+, \quad (2.3a)$$

$$\partial_t \rho_- - d_1 v_0 \nabla_x \cdot (\rho_- v(\bar{\theta})) + \frac{1}{T} \partial_s \rho_- = -\Lambda(\sigma_+, s) \rho_-, \quad (2.3b)$$

$$(\sigma_+ + \sigma_-) \partial_t \bar{\theta} + d_2 v_0 (\sigma_+ - \sigma_-) (v(\bar{\theta}) \cdot \nabla_x) \bar{\theta} + \mu v_0 v(\bar{\theta})^\perp \nabla_x (\sigma_+ - \sigma_-) = 0, \quad (2.3c)$$

supplemented by boundary conditions at the age $s = 0$,

$$\rho_+(x, 0, t) = T \int_0^\infty \Lambda(\sigma_+, s) \rho_- ds, \quad \rho_-(x, 0, t) = T \int_0^\infty \Lambda(\sigma_-, s) \rho_+ ds, \quad (2.4)$$

where the coefficients d_1 , d_2 and μ are given by (A.16), $\Lambda(\sigma, s)$ is defined in (2.2) and $\sigma_{\pm}(x, t)$ are the local masses of the two opposing groups:

$$\sigma_{\pm}(x, t) = \int_0^\infty \rho_{\pm}(x, s, t) ds.$$

Fig. 2(a) illustrates the reversal- and age-related dynamics of (2.3): For $s \in [0, 1]$, bacteria are in the refractory period and can not reverse, ensured by $\Lambda(\sigma_{\mp}, s) = 0$. For $s > 1$, bacteria enter the C-factor sensitive period and the reversal frequency is governed by the reversal function $\Lambda(\sigma_{\mp}, s) = \lambda(\sigma_{\mp})$. Assuming that there are in fact only two essential age states for the age variable s allows to simplify (2.3) to remove the age s as independent variable. This is done in the following section.

2.3 The 2-Age Model

To arrive at an easy-to-handle, yet powerful macroscopic model, we perform one last simplification step: we assume only two age groups, whose densities are denoted by $\rho_{\pm}^0(x, t)$

for C-signaling insensitive (refractory) bacteria and $\rho_{\pm}^1(x, t)$ for C-signaling sensitive bacteria. The main difference to the continuous-age model is that the aging itself is now described as a simple reaction term with rate $1/T$. Fig. 2(b) depicts the corresponding reaction schematic. The time evolution of the nematic mean direction remains unchanged. The derivation can be found in App. A.2 and the resulting system reads

$$\partial_t \rho_+^0 + d_1 v_0 \nabla_x \cdot (\rho_+^0 v(\bar{\theta})) = -\frac{1}{T} \rho_+^0 + \lambda(\sigma_+) \rho_-^1, \quad (2.5a)$$

$$\partial_t \rho_+^1 + d_1 v_0 \nabla_x \cdot (\rho_+^1 v(\bar{\theta})) = \frac{1}{T} \rho_+^0 - \lambda(\sigma_-) \rho_+^1, \quad (2.5b)$$

$$\partial_t \rho_-^0 - d_1 v_0 \nabla_x \cdot (\rho_-^0 v(\bar{\theta})) = -\frac{1}{T} \rho_-^0 + \lambda(\sigma_-) \rho_+^1, \quad (2.5c)$$

$$\partial_t \rho_-^1 - d_1 v_0 \nabla_x \cdot (\rho_-^1 v(\bar{\theta})) = \frac{1}{T} \rho_-^0 - \lambda(\sigma_+) \rho_-^1, \quad (2.5d)$$

$$(\sigma_+ + \sigma_-) \partial_t \bar{\theta} + d_2 v_0 (\sigma_+ - \sigma_-) (v(\bar{\theta}) \cdot \nabla_x) \bar{\theta} + \mu v_0 v(\bar{\theta})^\perp \nabla_x (\sigma_+ - \sigma_-) = 0, \quad (2.6)$$

where the local masses are given by $\sigma_{\pm} = \rho_{\pm}^0 + \rho_{\pm}^1$. The constants d_1 , d_2 and μ are defined analogously as for (2.3).

2.4 The Reversal Frequency $\lambda(\rho)$

To complete the models presented in Sec. 2.1-2.3, the density dependence of the reversal frequency $\lambda(\rho)$ has to be specified based on the available information from experiments. Firstly, in most experiments the number of reversals increase with the density of opposing bacteria, i.e. $\lambda'(\rho) \geq 0$. Next, in the absence of other bacteria isolated myxobacteria still reverse, i.e. $\lambda(0) =: \lambda_m > 0$. Spontaneous reversal rates between 0.07 and 0.09 reversals per minute have been reported [50, 53, 57]. Thirdly, there seems to be an upper limit as to how frequent reversals can be, which confirms the biological intuition that the rearrangement of the internal movement machinery takes some time. In [57] a maximal rate of 1.5 reversals per minute have been observed. Finally, [50] performed the experiments in which the reversal rate of isolated bacteria was measured in response to externally adding the signaling molecule C-factor, which was thought to communicate the density information. At low concentration of C-factor the reversal rate remained the same, while with increasing concentration a growth in reversal rate was observed, which plateaued for very high concentrations of C-factor. Using these pieces of information we assume a sigmoid shape of $\lambda(\rho)$. As a convenient representation we use a C^1 and piecewise smooth function (see Fig. 9A):

$$\lambda(\rho) = \begin{cases} \lambda_m + \frac{1}{2}(\lambda_M - \lambda_m) \left(\frac{\rho}{\bar{\rho}}\right)^2 & \text{if } \rho < \bar{\rho}, \\ \lambda_M - \frac{1}{2}(\lambda_M - \lambda_m) \left(\frac{\rho}{\bar{\rho}} - 2\right)^2 & \text{if } \bar{\rho} \leq \rho < 2\bar{\rho}, \\ \lambda_M & \text{elsewhere.} \end{cases}$$

Note that $\lambda(\rho)$ is parameterized by three quantities, the spontaneous reversal rate λ_m , the maximal reversal rate λ_M and the inflection density $\bar{\rho}$, at which $\lambda(\rho)$ grows the fastest.

3 Numerical Analysis - Comparison to Experiments

Depending on the precise experimental set-up, various bacterial speeds v_0 were observed [53, 60, 50], ranging from 2.7 to $11\mu\text{m}/\text{min}$. We do not have reliable biological data on the refractory period T and the inflection density $\bar{\rho}$. In [31] it was suggested that the refractory period must be less than 40 sec, while in [7] times around 5 min were suggested. We use $T = 1$ min, but note that our analysis shows wave synchronization also for any value larger than 40 sec. We fitted one parameter $\bar{\rho}$ to produce the correct ripple wavelength. A list of all parameters can be found in Tab. 1.

3.1 The particle model in 2D

As a first test of the model, we simulate the full 2D particle model described in Sec. 2.1. Details about the numerical method as well as simulation parameters can be found in App. A.3. Both the initial positions $X_i \in \mathbb{R}^2$ and the initial orientations $\Theta_i \in [-\pi, \pi)$ follow a uniform random distribution. The age variable was initialized with a uniform random distribution on $[0, 1]$, i.e. all bacteria are assumed to have reversed before the start of the simulation, however also other choices will lead to the same behavior.

The particle model shows ripple formation. Within about one hour an almost spatially constant nematic mean direction is established (in this simulation it is $\bar{\Theta} = 174^\circ$) and all bacteria are either aligned or anti-aligned with it, with small deviations caused by the noise. Just like in experiments, macroscopic traveling density bands develop, in which bacteria travel in the same direction as the band itself and normal to its longitudinal axis. Fig. 3(a) depicts the simulation outcome at time $t = 200$ min (see also SI video 1 for the whole time history of this simulation). To distinguish between bacteria aligned or anti-aligned with the (global) nematic mean direction, they are shown in red and blue respectively and in the following we will sometimes refer to them as *right- and left-moving* bacteria. The global ordering indicates that the nematic alignment quickly drives the system to a quasi 1D situation. To further analyze what happens along the nematic mean direction, we calculate the densities of the right- and left-moving bacteria within a thin strip in the simulation domain (Fig. 3(b) upper and middle figures). Additionally we examine the composition of each wave in terms of C-signaling sensitive and insensitive bacteria: the middle figure in Fig. 3(b) clearly shows the density waves and indicates that the wave composition is different before (box A) and after (box B) a wave crest collision. This will be examined further below.

Individual bacteria reverse upon crest collisions. From biological experiments it is known that when two waves meet, bacteria in the crests typically reverse their direction of movement. The macroscopic, experimental observations, i.e. that counter-propagating waves move with approximately the bacterial speed, persist over time and travel through each other seemingly unaffected, can be easily verified in Fig. 4, which shows a space-time plot of the total (1D) densities in the rectangular strip marked in Fig. 3(a) for $170 \text{ min} \leq t \leq 200 \text{ min}$. To examine the behavior of individual bacteria in this macroscopic context, Fig. 4(a) also shows the space-time path (blue) of three individual bacteria (marked

in Fig. 3(a)). Consistent with experiments, bacteria mostly reverse upon crest collision (e.g. particle path two or three) and rarely reverse between crest collisions (e.g. first path $t \approx 192$ min). This shows that the waves are mostly reflected off each other, confirming the accordion-like behavior known biologically.

The 2-age model is a good approximation of the particle model. The above results show that the particle model provides a faithful approximation of the biological reality. Since particle models come with a high computational cost and are inherently hard to analyze analytically, we want to use the much simpler 2-age model to gain biological insight into wave formation. Motivated by the observation that alignment leads to a *global* nematic mean direction, we assume $\bar{\theta} \equiv 0$ in the 2-age model, which amounts to setting $v(\bar{\theta}) = (1, 0)^T$ and omitting the equation for $\bar{\theta}$. We simulate (2.5) with randomly perturbed, constant initial conditions of equal mean density as the stripe in Fig 3 (see caption of Fig. 3 for details). Also in the 2-age model, opposing traveling waves emerge (discussed in more detail in Sec. 3.2). Fig. 3(b) compares the 1D densities calculated from the IBM to those of the 1D 2-age model: Both wavelengths and crest widths match closely. Further one can observe that the composition of the crests in terms of refractory and non-refractory bacteria match very well prior and after crest collision (boxes A and B in the middle and lower figures). Finally also the macroscopic wave behavior is very similar as can be observed in the space-time plots shown in Fig. 4. The remainder of the section is therefore devoted to analyzing the 1D 2-age model (2.5).

3.2 The wildtype: emergence of waves

We want to understand wave formation, shape and behavior in more detail using the 1D 2-age model (2.5). All simulations are performed with periodic boundary conditions on an interval of length $L = 500\mu m$ using the wildtype parameters listed in Table 1 (unless stated differently). The numerical method is discussed in App. A.3. Note that system (2.5) conserves the total mass and we define $2m_0$ as the average total density, which is constant in time:

$$2m_0 := \frac{1}{L} \int_0^L (\rho_+^0 + \rho_-^0 + \rho_+^1 + \rho_-^1) dx.$$

As initial conditions we use the spatially and temporal steady state solutions

$$\rho_+^0 = \rho_-^0 \equiv \frac{m_0 \lambda(m_0)}{1/T + \lambda(m_0)}, \quad \rho_+^1 = \rho_-^1 \equiv \frac{m_0 1/T}{1/T + \lambda(m_0)} \quad (3.7)$$

and perturb them with a uniform random distribution. These steady state solutions reflect the fractions of non-refractory and refractory cells in the absence of spatial patterning. Large reversal rates, i.e. large values of $\lambda(m_0)$ will increase the fraction of refractory cells, because cells will spend less time on average in a non-refractory state. Small refractory periods T on the other hand decrease them, as they will shortly become sensitive to C-signaling again.

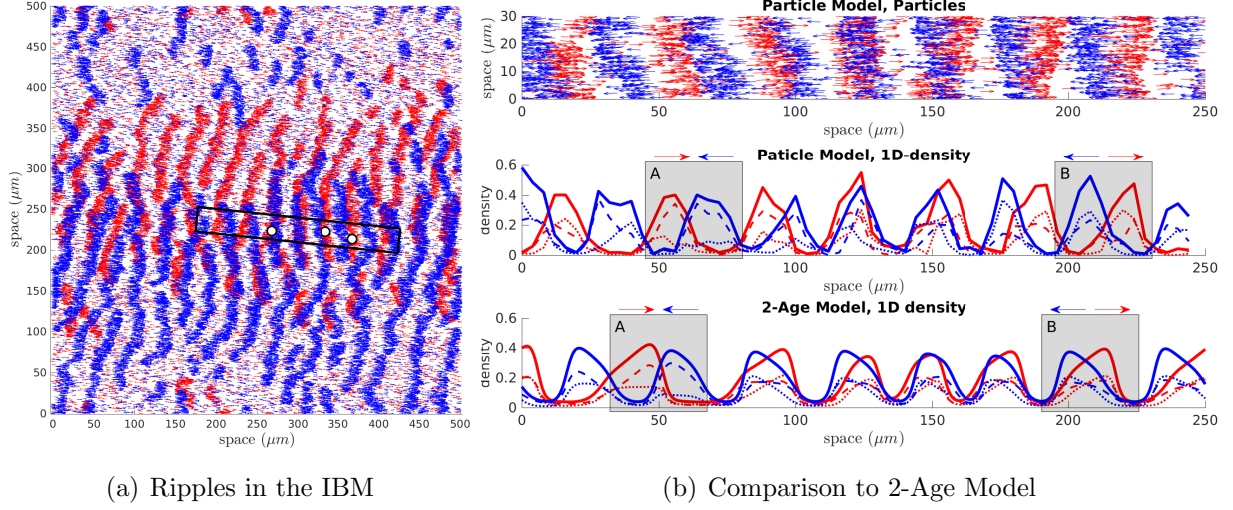


Figure 3: *Comparison IBM and 2-Age Model: Wave composition.* (a) shows the bacteria at time $t = 200$ min of a simulation of the IBM using uniform, random initial conditions (see also SI video 1 for the whole time history of this simulation). The nematic mean direction is almost globally constant with $\bar{\Theta} = 174^\circ$. Bacteria aligned and anti-aligned with it are depicted in red and blue respectively. (b) upper figure: The rectangular strip marked in (a) turned by the global nematic mean direction. (b) middle figure: The 1D-densities of right-moving (red) and left-moving (blue) bacteria calculated from the strip above with a grid-size of $4\mu m$ in x direction and averaging in y direction. Each wave consists of C-signaling insensitive, refractory bacteria ($s_i \leq 1$, dotted) and C-signaling sensitive, non-refractory bacteria ($s_i > 1$, dashed). Arrows mark the direction of movement of the crests. (b) lower figure: Simulation at time $t = 200$ min of the 1D 2-age model. For comparability with the stripe in (a) we chose the same mean density, i.e. we use as initial conditions for (2.5) $\rho_{\pm}^1(x, 0) \equiv 0.196/\mu m^2$ plus/minus a uniform random perturbation of magnitude $0.02\mu m^{-2}$ and set $\rho_{\pm}^0(x, 0) \equiv 0$. Color and line-styles are the same as in middle figure. Boxes A and B mark crests before (A) and after (B) collisions for both the IBM and the 2-age model.

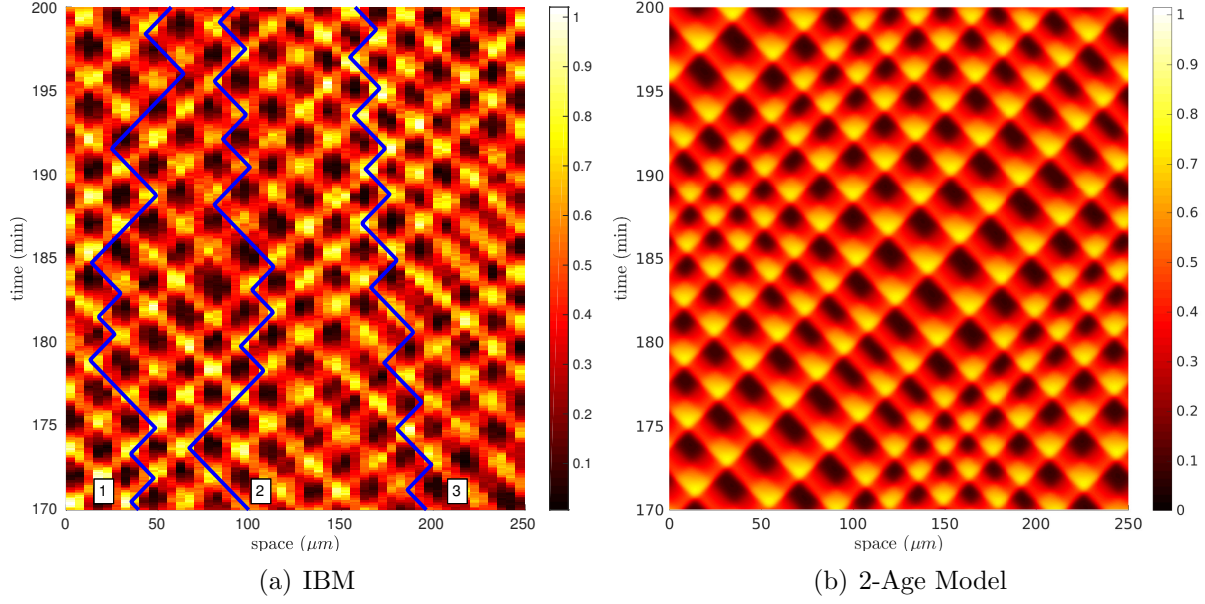


Figure 4: *Comparison between IBM and 2-Age Model: Wave behavior.* (a) shows the 1D densities along the rectangular strip marked in Fig. 3(a) calculated at each time step for $170 \text{ min} \leq t \leq 200 \text{ min}$. It can be seen that waves persist over time, move with a speed of $\approx 9 \mu\text{m}/\text{min}$ and are not affected by collisions. Blue lines are the traces of the three particles marked in Fig 3(a). They mostly travel in wave crests, typically reverse upon wave collision and make almost no net movement along the strip. (b) depicts the densities over the same time interval for the 1D 2-age model showing very similar macroscopic behavior. The units of both colorbars are bacteria per μm^2 .

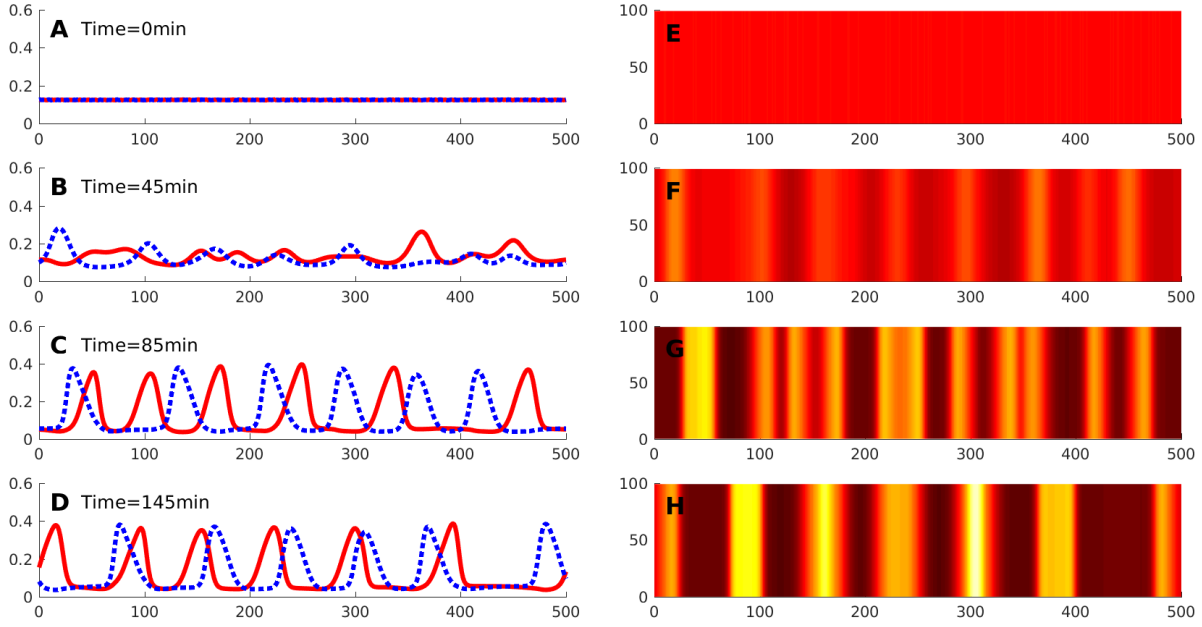


Figure 5: *Ripple Emergence*. A-D: Time snapshots of the densities σ_{\pm} of right-moving bacteria (red-solid) and left-moving bacteria (blue-dotted). The x-axis is in μm and the y-axis is in bacteria per μm^2 . E-G: "Microscopy-view", from above. The total local density of bacteria $\sigma_+ + \sigma_-$ is shown in 2D space at the same time points as A-D. All length units are μm .

In Fig. 5 a time series of one simulation is shown. After about one hour bands of oppositely moving ripples start to develop and are fully established after two hours, after which their general shape and speed do not change anymore. The ripple crests move with a speed close to the bacterial speed ($8.8 \mu m/min$) to the left and right respectively. The density ratio between crests and troughs is about 10, which corresponds to the experimental values found e.g. in [50]. Upon collisions of two such waves, the total bacteria densities (Fig. 5E-H) double, as described also in experiments. The shapes of the individual waves of left- and right-moving bacteria themselves seem to be almost unaffected by the collision, with only slight deformations. However, when inspecting the composition of the ripple crests in terms of refractory and non-refractory bacteria during a collision, one can observe two distinct phases: a *collision phase* and a *reconstitution phase* (see Fig. 6): while before the collision the fraction of refractory bacteria is low, it increases rapidly in the collision phase, indicating a high number of reversals taking place. In the reconstitution phase that follows, this fraction decreases again and resumes its original value. During this phase, the C-signal insensitive bacteria go through their refractory period and "age" back into C-signaling sensitive bacteria. To estimate the fraction of bacteria that reverse during a collision, we compare the total number of reversing bacteria in one wave in the course of one collision to the original number of bacteria present in that wave before the collision. Fig. 6 (left, solid line) shows that essentially all bacteria reverse, i.e. the wave is almost fully reflected. Note that this count includes reversing bacteria that originally moved with the other wave, however, it takes those at least $T + 2/\lambda_M = 2.3$

min to reverse, age and reverse again, which is almost the duration of the full collision, showing that they hardly contribute.

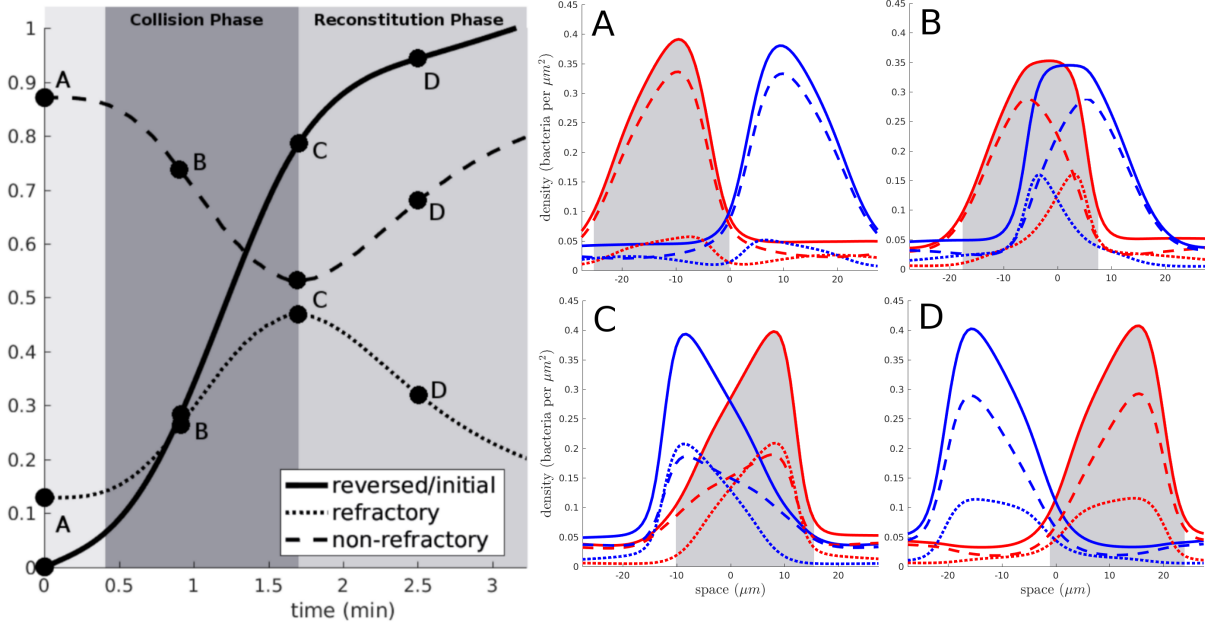


Figure 6: *Collision Study*. Left: The fraction of refractory (dotted) and non-refractory (dashed) bacteria in the wave over the time of one collision. The solid line shows the cumulative, total number of reversing bacteria in that wave as a fraction of the total number of bacteria originally present. The extent of the wave crest is defined by $\sigma_{\pm} \geq 0.1$ (see gray shaded regions in Fig. A-D on the right). Dots mark the time points that are shown to the right. Right A-D: Time snapshots showing densities of refractory (dotted) and non-refractory (dashed) cells as well as their sum (solid) for the left- and right-moving groups (blue and red respectively). Parameters are listed in Table 1.

3.3 The influence of the refractory period T

A memory-free model still produces traveling waves. A crucial part of the presented model is the introduction of the refractory period T . What is its influence on the bacterial behavior predicted by the 2-age model? In order to assess this, we investigate what changes in the absence of T . The corresponding model can be interpreted as a *memory-free* model, as bacteria retain no information about their previous reversals (see explanation below). Mathematically this can be realized by taking the limit $T \rightarrow 0$, i.e. bacteria are susceptible to C-signaling immediately after they reverse. System (2.5) then reduces to $\rho_{\pm}^0 \equiv 0$ and $\rho_{\pm}^1 = \sigma_{\pm}$ fulfilling (compare with Fig. 2(c) for the reaction diagram)

$$\partial_t \rho_+^1 + d_1 v_0 \nabla_x \cdot (\rho_+^1 v(\bar{\theta})) = \lambda(\rho_+^1) \rho_-^1 - \lambda(\rho_-^1) \rho_+^1, \quad (3.8a)$$

$$\partial_t \rho_-^1 - d_1 v_0 \nabla_x \cdot (\rho_-^1 v(\bar{\theta})) = \lambda(\rho_-^1) \rho_+^1 - \lambda(\rho_+^1) \rho_-^1, \quad (3.8b)$$

$$(\rho_+^1 + \rho_-^1)\partial_t \bar{\theta} + d_2 v_0 (\rho_+^1 - \rho_-^1)(v(\bar{\theta}) \cdot \nabla_x) \bar{\theta} + \mu v_0 v(\bar{\theta})^\perp \nabla_x (\rho_+^1 - \rho_-^1) = 0. \quad (3.9)$$

Remark 3.1 *The formally correct way to derive this system requires two steps: Firstly, system (2.5) needs to be non-dimensionalized by introducing a suitable reference timescale \bar{t} . A natural choice is $\bar{t} = \frac{L}{d_1 v_0} \approx 57$ min, i.e. the time it would take a non-reversing bacteria to cross the domain. The above limit then amounts to saying that $\varepsilon = T/\bar{t}$ is small compared to this typical time scale. Secondly, one needs to Taylor expand the functions ρ_\pm^0 and ρ_\pm^1 in terms of ε . One then finds that to the first order ρ_\pm^0 are zero and ρ_\pm^1 fulfill system (3.8).*

This system has already been described in [20], where a memory-free myxobacteria model without an internal age variable s was derived. Note that without the reaction term (i.e. $\lambda \equiv 0$), the system describes the macroscopic limit of purely nematic interactions, a phenomena of great interest in physics and studied in various works [27, 48, 46, 22]. Assuming a constant nematic direction $\bar{\theta}$, the system reduces to two coupled transport-reaction equations; equations of this type were examined in the context of pattern formation and aggregation in biological systems e.g. in [25, 39] (see also the discussion below).

We simulate the memory-free model (3.8) in one space dimension (assuming $\bar{\theta} \equiv 0$), with the same parameters as for the 2-age model (Tab. 1) and observe that the constant steady state again destabilizes under randomly perturbed initial conditions and traveling bumps occur. However, their widths vary greatly and do not seem to be controlled by the dynamics at all. In fact in [39] it was commented that the system seems to converge to piecewise constant traveling waves, traveling precisely at speed $d_1 v_0$, which fulfill (3.8) in a weak sense.

The refractory period causes wave synchronization. The results from the memory-free model suggest that while the refractory period might not be necessary for the formation of opposing traveling waves, it seems to be responsible for controlling the width of the individual traveling crests and synchronizes the waves by controlling the wavelength. To examine this further we systematically vary T in the 2-age model and examine the effect. In Fig. 7 it can be observed that there are two parameter regimes. For very small refractory periods, the system behaves similar to the memory-free, limiting system (3.8), i.e. while traveling waves occur, the crest width and wavelength varies greatly, indicating a lack of synchronization. After reaching a critical value of $T \approx 0.8$ min the waves become more synchronized and the crests share a common width. In this regime larger refractory periods lead to wider crests with larger wavelength. How can we interpret these results?

Recent collisions cause asymmetric wave reflection. The reason for the lack of synchronization in the case of small T lies in the fact that bacteria retain no memory of previous reversals, hence two waves cannot affect each other. To understand how the refractory period enhances wave synchronization, it is instructive to look again at Fig. 6: as described above, during the reconstitution phase after a collision, the number of

non-refractory cells grows back to its equilibrium value. This growth depends on T (the smaller T , the faster the growth). If now the crest meets another crest before sufficiently many bacteria have regained their sensitivity to the C-factor, the wave will not be fully reflected off the oncoming wave. Fig. 8 depicts the result of a simulation, in which one right-moving wave meets two left-moving waves traveling with a short wavelength for both the 2-age model (A-D) and the memory-free model (F-I). Fig. 8E and J depict how many bacteria reverse on average in each wave per minute (i.e. to be precise, if x_a and x_b mark the beginning and end positions of a wave, Fig. 8E/J depict $1/(x_b - x_a) \int_{x_a}^{x_b} \lambda(\sigma_{\mp}) \rho_{\pm}^1 dx$ in both models). At the first collision the same (high) number of bacteria reverse in both waves, the waves are reflected off each other and the number of reversing bacteria is similar for both the 2-age model and the memory-free model. In the second collision for the 2-age model, however, the right-moving wave contains much fewer non-refractory cells (i.e. ρ_+^1 is lower) than the second left-moving wave, hence it is only partially reflected. The overall effect is a significant reduction of the second left-moving wave. For the memory-free case, the second collision resembles exactly the first collision, hence the second wave is unchanged.

3.4 Parameter-dependence on wave formation

Two necessary wave conditions. In many experimental set-ups, one of the main output is whether or not myxobacteria colonies form waves. We therefore examine what parameter combinations lead to wave formation. The previous section suggests that the length of the refractory period T has no influence on the appearance of waves. We therefore perform a rough parameter scan over the shape parameters of the reversal function $\lambda(\rho)$, i.e. the spontaneous reversal rate λ_m , the maximal reversal rate λ_M and the inflection density $\bar{\rho}$. Rigorous mathematical stability analysis of system (2.5) will give more insight into the precise stability regions also for other shapes of $\lambda(\rho)$ and will be the subject of future work. However, several conclusions can already be drawn. We find two wave formation conditions:

Condition A: The maximal reversal rate needs to be large enough compared to the spontaneous reversal rate ($\lambda_M > 3\lambda_m$).

Condition B: The inflection density and the average total density need to be of similar order ($\bar{\rho} \approx m_0$).

How can we link this to experiments?

Remark 3.2 *A non-dimensionalization of the system shows that its behavior depends on four dimensionless quantities*

$$\frac{d_1 v_0 T}{L}, \quad \frac{\lambda_m L}{d_1 v_0}, \quad \frac{\lambda_M L}{d_1 v_0} \quad \text{and} \quad \frac{\bar{\rho}}{m_0}.$$

Examining λ_m , λ_M and $\bar{\rho}$ therefore amounts to analyzing the last three quantities.

Mutation experiments: hypo- and hyper-reversing bacteria. To assess how the reversal behavior impacts the ripple formation, Sager and Kaiser have used *M. xanthus* strains, that have an insertion mutation in the *frzCD* gene, which has been shown

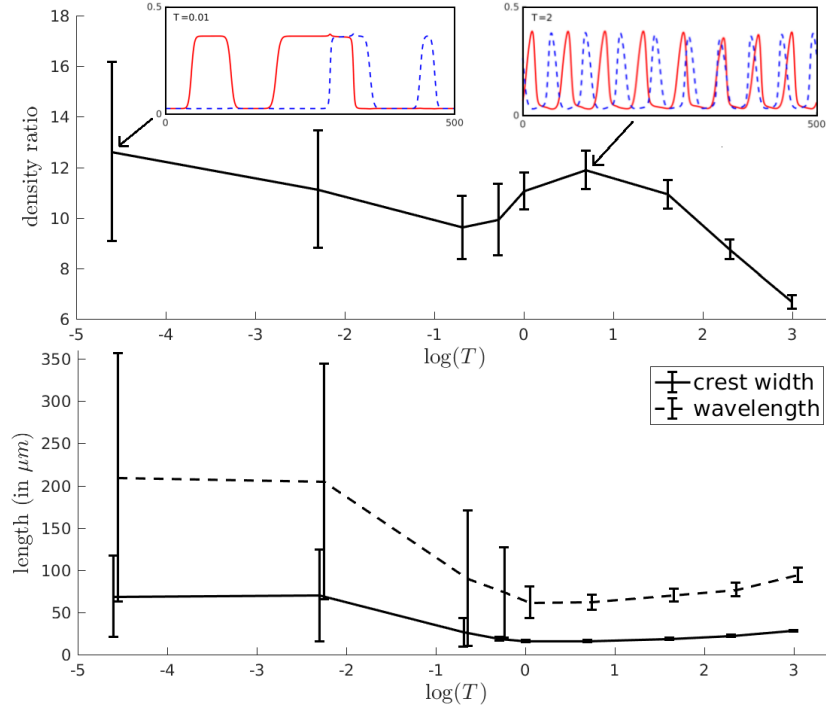


Figure 7: *Varying the refractory period T .* Shown are the dependencies of the density ratio between wave crest and wave trough (upper figure) and the wavelength and crest width (lower picture) on the refractory period T . Error bars show \pm standard deviation for a sample consisting of all waves from ten simulation runs per T . In the case of non-periodic waves, wavelengths were measured as distance of the center of masses of each crest. Insets in the upper picture depict the space dependent total densities σ_+ (red-solid) and σ_- (blue-dashed) at time 7 hrs of two simulation runs with $T = 0.01$ and 2 min. Measured are the shapes after the system has reached equilibrium, which takes up to 30 hrs for large values of T . Other parameters are listed in Tab. 1.

to impact the reversal probability [50]. Isolated individuals of the *hypo-reverses* change direction on average only 0.001 times per minute and *hyper-reversers* 0.455 times per minute (as compared to 0.09 times in the wildtype). Both strains have lost the ability to form ripples and it is suggested that the mutation affects the spontaneous reversal rate. To model this situation we have to ask which parameters are affected by the mutation. The observation that the refractory period does not affect wave formation suggests that T is ruled out, hence either λ_m or both λ_m and λ_M are affected. We assume that mutations change the reversal probability by shifting up $\lambda(\rho)$ in case of the hyper-reversers (such that $\lambda_m = 0.455/\text{min}$) and down in case of the hypo-reversers (such that $\lambda_m = 0.001/\text{min}$); see Fig. 9. Our simulations show that in both mutant strains the ability to form ripples is seriously impacted: hyper-reversers fail to form any kind of spatial patterning and the distribution of bacteria stays uniform. This can be explained by observing that wave condition A from above is violated. For hypo-reversers on the other hand, the steady state distribution is destabilized, however the developed patterns range from large traveling masses to very irregular crests (see Fig. 9).

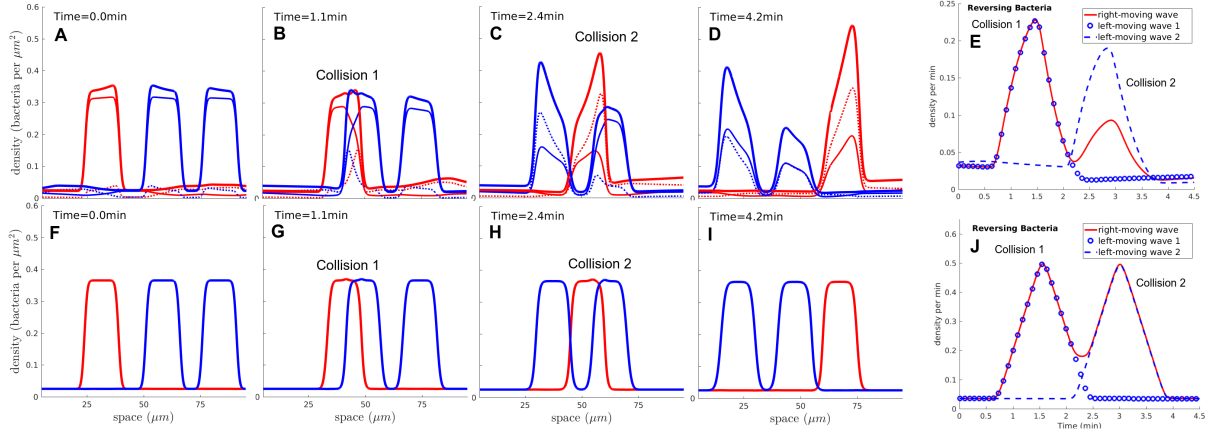


Figure 8: *Wavelength control*. A-D and F-I: Four time snapshots from a 1D-simulation with refractory period (i.e. system (2.5), A-D) and without (i.e. system (3.8), F-I). Shown are densities of non-refractory cells (thin-solid), refractory cells (thin-dashed), as well as their sums (thick-solid). Right- and left-moving densities are shown in red and blue, respectively. E and J: Average number of reversing bacteria per time in each of the three waves for the 2-age model (E) and the memory-free model (J) as a function of time, i.e. the average of $\lambda(\sigma_-)\rho_+^1$ (red-solid for right moving wave) and $\lambda(\sigma_+)\rho_-^1$ (blue-circles for leading left-moving wave and blue-dashed for following left-moving wave) over the whole wave. Parameters as in Tab.1 with $T = 4$ min for the 2-age model.

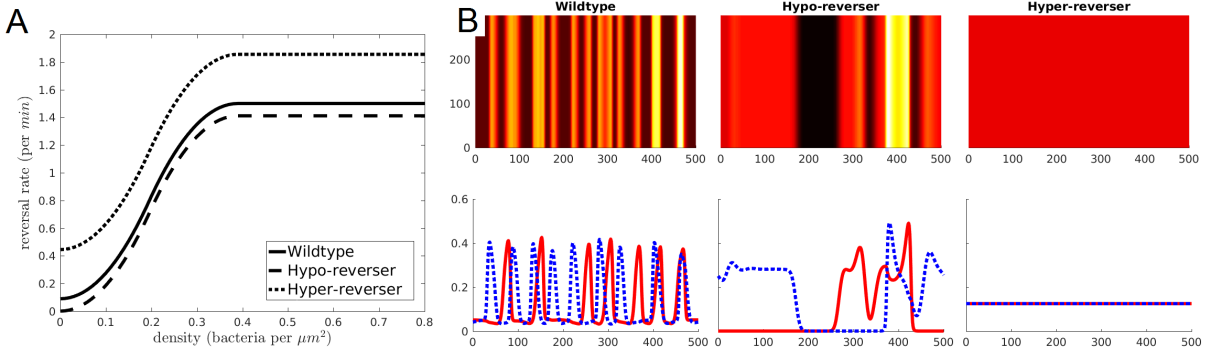


Figure 9: *Hypo and Hyper-reversers*. A: The reversal rate $\lambda(\rho)$ in dependence on the density of opposing bacteria for wildtype, hypo- and the hyper-reversing bacteria. B: Simulation outcome at time $t > 2$ hrs. Lower row: Right-moving bacteria (σ_+ , red-solid) and left-moving bacteria (σ_- , blue-dashed). Upper row: "microscopy-view", i.e. the total density $\sigma_+ + \sigma_-$ visualized in 2D space.

Dilution experiments: changing the fraction of C-signal competent cells.

Another way to demonstrate the influence of C-signaling on the ripple formation was a second set of experiments performed by Kaiser and Sager [50]: two strains of myxobacteria were used, a C-signaling competent wildtype strain $csgA^+$ and a mutant strain $csgA^-$, which can not produce C-signal, but can respond to it. By themselves ensembles of

csgA⁻ cells do not have the ability to form ripples. In their experiments Kaiser and Sager changed the fraction of *csgA*⁺ and *csgA*⁻ cells and measured the changes in ripple wavelength, speed and width. To simulate this situation using our 2-age model, one has to note that, since *csgA*⁻ cells react to C-signals in the same manner as the wildtype, the ratio between *csgA*⁺ and *csgA*⁻ will be constant everywhere. This was confirmed in [50]. For our model, this means that if the fraction of C-signaling competent *csgA*⁺ cells is $q \in [0, 1]$, one simply has to change $\lambda(\sigma_{\pm})$ to $\lambda(q\sigma_{\pm})$ in system (2.5), which in fact just changes $\bar{\rho}$ to $\bar{\rho}/q$. In view of wave condition B, this suggests that if q is too small, this would inhibit wave formation. This is in agreement with the experiments described in [50], although it should be noted that for very small fractions of *csgA*⁺ cells, for which waves were still present in the experiment, the corresponding large values of $\bar{\rho}$ do not produce waves anymore in our model. We further study how varying the inflection density $\bar{\rho}$ affects the wave shape (within the range that supports ripple formation). Fig. 10 depicts the impact on various wave characteristics. Wave speed is not affected and stays close to the individual bacterial speed. Crest width increases, as does ripple wavelength, both of which are in agreement with the findings in [50]. Our model also predicts a non-monotonous dependence of the ratio of the number of cells in the crest to the number of cells in the trough as a function of $\bar{\rho}$ (Fig. 10, upper-right), which could easily be addressed experimentally.

4 Discussion

We presented a novel, continuous, age-structured macroscopic model of myxobacteria, derived systematically from an individual-based model. The main assumptions of the model are nematic alignment, a density-dependent reversal function and a refractory period of fixed length, which introduces a memory effect.

In excellent agreement with experimental data on myxobacteria, simulations of the full IBM show the development of periodic waves, traveling in opposing directions and being reflected upon collision. We performed an in-depth numerical investigation of the one-dimensional macro-model for the case of two sensitivity/age groups: refractory cells, incapable of reversing, and non-refractory cells, that can reverse and are sensitive to C-signaling. A main result of our analysis is that the refractory period is not responsible for wave formation, but for wave synchronization. This is because it introduces a memory effect, that inhibits waves forming within a short distance to each other. The existence of a refractory period is known for example for *D. discoideum* [51, 55]. The idea of a refractory period for myxobacteria has originally been brought forward in the model presented in [31], where it is suggested that myxobacteria also go through an insensitivity period following a reversal. Assuming that the length of the refractory period is unaffected by the density of opposing bacteria, we show that the memory effect introduced by a fixed refractory period is sufficient to explain ripple synchronization. We discovered two wave formation conditions that are consistent with experimental results: the maximal reversal rate needs to be large enough compared to the spontaneous reversal rate and the average density of the myxobacteria colony needs to be close to $2\bar{\rho}$ with $\bar{\rho}$ being the inflection density at which the reversal function reacts the most sensitively to density changes.

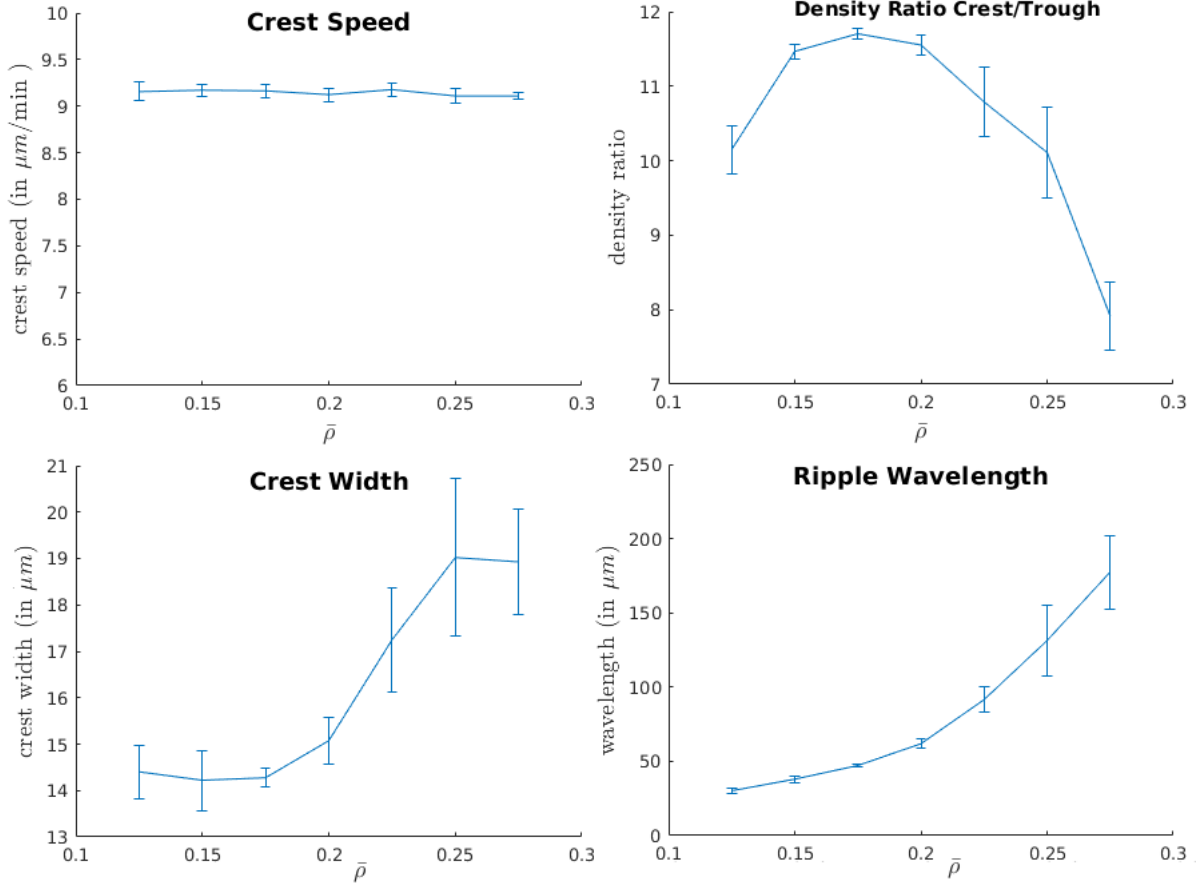


Figure 10: *Varying the inflection density $\bar{\rho}$.* The effect of varying $\bar{\rho}$ on various wave characteristics. Depicted are mean \pm standard deviation for all waves for 10 simulation runs per $\bar{\rho}$. Crest speeds were measured over the time that it takes for one wave to cross the simulation domain. Other parameters are listed in Tab. 1.

This predicts that both very high and very low densities will inhibit wave formation in myxobacterial colonies.

A strength of the Self-Organized Hydrodynamics (SOH) models is that they are directly derived from the corresponding IBM by the method of Generalized Collision Invariants (GCI). This allows for easy and transparent inclusion of assumptions, such as the density-dependent reversal rate and the refractory period. The simulations presented in Sec. 3.1 show good agreement between the IBM and 2-age model, however, to fully validate the correspondence between the macroscopic model and the IBM, further simulation and tests will be necessary. However for similar problems of collective behavior the SOH models have been proven to provide an accurate approximation of particle dynamics [44, 15, 23]. In this work we concentrated on wave formation, where both experimental results and particle simulations suggest that the dynamics can be studied in one space dimension. However, several other macroscopic patterns are known for myxobacteria, most notably the formation of large aggregates. The combination of simulation results of both the IBM and the two-dimensional 2-age model as well as analytical results of

the latter might shed light on what parameters cause cells to switch between a uniform state to ripple formation and aggregation. Several aspects will need to be considered: could the reversal frequency depend on both the densities of the opposing group as well as on the aligned one? In [39] such cases were analyzed for a memory-free model and simulations also showed wave formation. Further [39] also noted that small changes in the reversal function $\lambda(\rho)$ can cause the system to switch from ripples to aggregation. It will be interesting to extend the results to the age-structured model. In [34] experiments were described in which C-signaling and thereby local densities affect the gliding speed of bacteria. Such density-dependent parameters can easily be incorporated into SOH models and significantly impact the dynamics [26].

A large number of IBMs exist for self-propelled particles such as myxobacteria [53] and detailed numerical and statistical analysis of their properties have significantly contributed to the understanding of emergent phenomena and phase transitions. While they allow for direct comparison between the experimental data about the behavior of the individuals, they are limited in terms of insights into macroscopic phenomena. For macro-systems such as the 2-age model on the other hand, stability or asymptotic analysis can be performed which can elucidate precise parameter dependencies and long-term behavior. The macro-system of [31] triggered a number of works examining wavelength determination [6, 32], demonstrating the potential insight gained through analytical methods. For the macro-system presented here, a rigorous analytical treatment will be the subject of future work. Several works deal with the linkage between IBMs and meso- or macro-models, e.g. both in [7] and [28] where continuous models are derived from particle models. The methods presented there as well as the GCI method offer a powerful option of combining the strengths of both particle and continuous based methods.

Our work together with the results in [31, 7, 53] strongly suggests the existence of a refractory period. Several aspects of our findings can be addressed experimentally: our main results is that wave formation and wave synchronization are independent phenomena, which would suggest separate molecular mechanisms. We therefore predict that mutants that form non-synchronized traveling waves of various width have a density-dependent reversal frequency, but no refractory period. As to the length of the refractory period, in [31] experimental data argued for refractory periods of under 1 min. Our model argues that $T \approx 50$ sec presents the lower limit for the formation of synchronized waves, larger refractory periods also lead to periodic waves, but it takes the system much longer to produce steadily moving wave. Hence the value $T \approx 50$ sec is the fastest way to make synchronized waves, presenting a possible, evolutionary answer as to why this particular refractory period length evolved.

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Data availability

No new data were collected in the course of this research.

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A Appendix

A.1 Derivation of the Macroscopic Continuous-Age Model (2.3)

The particle model presented in Sec. 2.1 serves as the starting point for the derivation. We largely follow [20] and emphasize differences where appropriate.

Kinetic Equation. Following the classical strategy for mean field models, presented e.g. in [21], we let the number of particles N tend to infinity. Then the distribution function $f(x, \theta, s, t)$ satisfies the following Kolmogorov-Fokker-Planck type equation:

$$\partial_t f + v_0 \nabla_x \cdot (v(\theta) f) + \frac{1}{T} \partial_s f = Q_{\text{al}}^R(f) + Q_{\text{rev}}^R(f).$$

We recall that R denotes the interaction radius for both reversals and alignment. Here and in the following the superindex R is used to emphasize the non-locality of the corresponding terms. The collision operator Q_{al}^R , caused by the alignment is almost identical to that derived in [20] and is given by

$$Q_{\text{al}}^R(f) = \partial_\theta \left[\nu \text{Sign}(\cos(\theta - \bar{\theta}_f^R)) \sin(\theta - \bar{\theta}_f^R) f + D \cos^2(\theta - \bar{\theta}_f^R) \partial_\theta f \right],$$

where the nematic mean direction $\bar{\theta}_f^R$ is defined by

$$v(2\bar{\theta}_f^R(x, t)) = \frac{J_f^R(x, t)}{|J_f^R(x, t)|}, \quad \text{with } J_f^R(x, t) = \int_0^\infty \int_{|x-y| \leq R} \int_{-\pi}^\pi v(2\theta) f(y, \theta, s, t) dy d\theta ds.$$

Note that the definition of the mean nematic current J_f^R requires integrating over all ages s , a small difference to the operator of the age-free model defined in [21], which reflects the fact that the biochemical age of a bacterium does not influence the alignment. The

first term in Q_{al}^R is a drift term in θ that moves the mass towards $\bar{\theta}_f^R$ and $\bar{\theta}_f^R - \pi$. The second term causes diffusion in θ with magnitude $D \cos^2(\theta - \bar{\theta}_f^R)$.

The new operator $Q_{\text{rev}}^R(f)$, describes the reversals and is defined as follows. First we introduce two quantities $\sigma_f^{R,\pm}(x, t)$ representing the position-dependent, total densities of each group,

$$\sigma_f^{R,\pm}(x, t) = \frac{1}{\pi R^2} \int_0^\infty \int_{\pm \cos(\theta - \bar{\theta}_f^R) > 0} \int_{|x-y| \leq R} f(y, \theta, s, t) dy d\theta ds.$$

Then we have

$$Q_{\text{rev}}^R(f) = - \left[\Lambda(\sigma_f^{R,-}, s) \chi_{\{\cos(\theta - \bar{\theta}_f^R) > 0\}} + \Lambda(\sigma_f^{R,+}, s) \chi_{\{\cos(\theta - \bar{\theta}_f^R) < 0\}} \right] f(x, \theta, s, t), \quad (\text{A.10})$$

where $\chi_{\mathcal{S}}$ is the characteristic function on the set \mathcal{S} and $\Lambda(\sigma, s)$ is defined in (2.2). (A.10) is nonzero only for $s > 1$, since only then particles are sensitive to C-signaling and can reverse with a frequency that depends on the density of the opposing group. Note that (A.10) represents particles reversing *away* from their group; those *entering* a group are accounted for as boundary conditions at the age $s = 0$ given by

$$f(x, \theta, 0, t) = T \int_0^\infty \left(\Lambda(\sigma_f^{R,-}, s') \chi_{\{\cos(\theta - \bar{\theta}_f^R) < 0\}} + \Lambda(\sigma_f^{R,+}, s') \chi_{\{\cos(\theta - \bar{\theta}_f^R) > 0\}} \right) f(x, \theta + \pi, s', t) ds'.$$

The integral reflects the fact that reversing particles of all ages that point in direction $\theta + \pi$, will add mass to the distribution function at angle θ and age $s = 0$, since reversing resets the biochemical age to zero.

Scaling. Analogous to [20], we perform the nondimensionalization and the hydrodynamic scaling in one step. On the microscopic scale the reference time and space units are given by $t_0 = 1/\nu$ and $x_0 = v_0 t_0$. The age variable s remains unchanged since it is already dimensionless. The scaled diffusion constant is $d = D t_0$. On the macroscopic scale we use the coarse units $t'_0 = t_0/\varepsilon$, $x'_0 = x_0/\varepsilon$ where $\varepsilon > 0$ is some small real number. Then the dimensionless macroscopic variables are $\hat{t} = \frac{t}{t'_0}$, $\hat{x} = \frac{x}{x'_0}$. Further we set $\hat{R} = \frac{R}{x'_0}$. The scaled distribution function \hat{f} and densities $\hat{\sigma}_f^{\hat{R},\pm}$ are given by

$$\hat{f}(\hat{x}, \theta, s, \hat{t}) = \frac{f(x, \theta, s, t)}{(1/x'_0)^2} \quad \text{and} \quad \hat{\sigma}_f^{\hat{R},\pm}(\hat{x}, \hat{t}) = \frac{\sigma_f^{R,\pm}(x, t)}{(1/x'_0)^2}.$$

For the reversal term, we set $T = \hat{T} t'_0$ and $\hat{\Lambda}(\hat{\sigma}_f^{\hat{R},\pm}, s) = \Lambda(\sigma_f^{R,\pm}, s) t'_0$. Note that $\bar{\theta}_f^{\hat{R}}(\hat{x}, \hat{t}) = \bar{\theta}_f^R(x, t)$. At this point the definitions of the nematic mean direction and the densities $\hat{\sigma}_f^{\hat{R},\pm}$ still involve space integrals, i.e. they are non-local. We assume purely local interactions for both alignment and reversals and therefore set $\hat{R} = \varepsilon r$ with $r = \mathcal{O}(1)$. Then Taylor expansion of $\bar{\theta}_f^{\varepsilon r}$ and $\hat{\sigma}_f^{\varepsilon r,\pm}$ around $\varepsilon = 0$ shows that the functions can be approximated by the local-in-space functions $\bar{\theta}_{\hat{f}}$ and $\hat{\sigma}_{\hat{f}}^\pm$ respectively (see (A.12), (A.13)) with a remainder of order $\mathcal{O}(\varepsilon^2)$. In the following we drop the hats for better readability.

Hydrodynamic Limit. To derive the mean field equation, we need to find the solution $f^\varepsilon(x, \theta, s, t)$ as $\varepsilon \rightarrow 0$ in

$$\varepsilon(\partial_t f^\varepsilon + \nabla_x \cdot (v(\theta) f^\varepsilon) + \frac{1}{T} \partial_s f^\varepsilon) = Q_{\text{al}}(f^\varepsilon) + \varepsilon Q_{\text{rev}}(f^\varepsilon). \quad (\text{A.11})$$

where

$$Q_{\text{al}}(f) = \partial_\theta [\text{Sign}(\cos(\theta - \bar{\theta}_f)) \sin(\theta - \bar{\theta}_f) f + d \cos^2(\theta - \bar{\theta}_f) \partial_\theta f]$$

and

$$\begin{aligned} Q_{\text{rev}}(f) = & \int_0^\infty \left(\Lambda(\sigma_f^-(x), s') \chi_{\{\cos(\theta - \bar{\theta}_f) < 0\}} + \Lambda(\sigma_f^+(x), s') \chi_{\{\cos(\theta - \bar{\theta}_f) > 0\}} \right) f(x, \theta + \pi, s', t) ds' \delta(s) \\ & - \left(\Lambda(\sigma_f^-(x), s) \chi_{\{\cos(\theta - \bar{\theta}_f) > 0\}} + \Lambda(\sigma_f^+(x), s) \chi_{\{\cos(\theta - \bar{\theta}_f) < 0\}} \right) f(x, \theta, s, t), \end{aligned}$$

where $\delta(s)$ is the Dirac-delta distribution. Note that we included the boundary condition at $s = 0$ into the definition of Q_{rev} . The mean nematic direction is defined by

$$v(2\bar{\theta}_f(x, t)) = \frac{J_f(x, t)}{|J_f(x, t)|}, \quad \text{with } J_f(x, t) = \int_0^\infty \int_{-\pi}^\pi v(2\theta) f(x, \theta, s, t) d\theta ds. \quad (\text{A.12})$$

and the local mass functions are

$$\sigma_f^\pm(x, t) = \int_0^\infty \int_{\pm \cos(\theta - \bar{\theta}_f) > 0} f(x, \theta, s, t) d\theta ds. \quad (\text{A.13})$$

Taking the hydrodynamic limit in the SOH framework [21] now involves two steps: (i) Characterizing the kernel of $Q_{\text{al}}(f)$ (θ dependence) and (ii) Using Generalized Collision Invariances (GCIs) to extract information about the x and t dependence from the transport and reversal terms.

Step (i): Since $Q_{\text{al}}(f)$ is identical to the collision operator analyzed in [20], we simply cite the result:

Lemma A.1 *The kernel of Q_{al} is given by*

$$\{\bar{f}_{\rho_+, \rho_-, \bar{\theta}}(\theta) | (\rho_+, \rho_-) \in [0, \infty)^2, \bar{\theta} \in [0, \pi)\},$$

where

$$\bar{f}_{\rho_+, \rho_-, \bar{\theta}}(\theta) = \begin{cases} \rho_+ M_{\bar{\theta}}(\theta) & \text{for } \cos(\theta - \bar{\theta}) > 0 \\ \rho_- M_{\bar{\theta}}(\theta) & \text{for } \cos(\theta - \bar{\theta}) < 0. \end{cases} \quad (\text{A.14})$$

$M_{\bar{\theta}}(\theta)$ describes the Generalized von Mises (GVM) distribution defined by

$$\begin{aligned} M_{\bar{\theta}}(\theta) &= \frac{1}{Z_d} \exp\left(-\frac{1}{d|\cos(\theta - \bar{\theta})|}\right), \quad \theta \in [-\pi, \pi) \\ \text{where } Z_d &= \int_{\cos \theta > 0} \exp\left(-\frac{1}{d \cos \theta}\right) d\theta. \end{aligned}$$

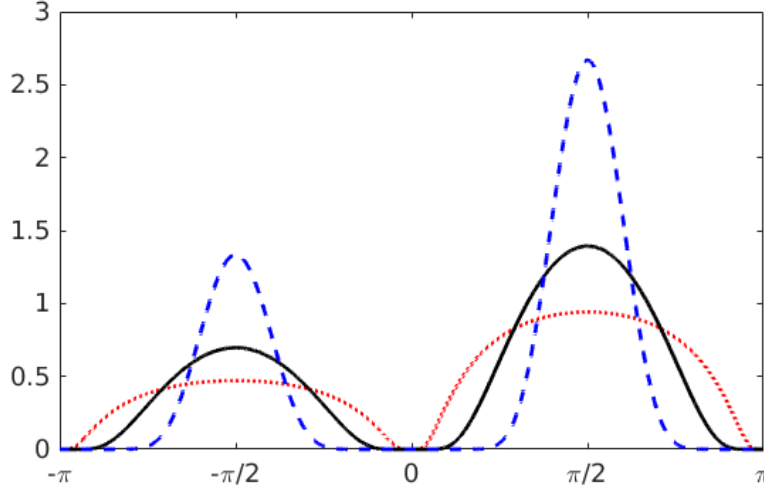


Figure 11: *Equilibria of Q_{al} .* The equilibrium distribution \bar{f} as defined in (A.14) for $(\rho_+, \rho_-, \bar{\theta}) = (2, 1, \pi/2)$ using $d = 2, 0.5$ and 0.1 (red-dotted, black-solid and blue-dashed respectively).

The equilibria have the shape of two opposing maxima: One in direction $\bar{\theta}$ with mass ρ_+ and one in direction $\bar{\theta} - \pi$ with mass ρ_- and are depicted in Fig. 11.

Step (ii): In a classical setting, one would at this point multiply equation (A.11) with collision invariants (CIs) and integrate over all directions θ . A CI is defined as a function $\Psi(\theta)$ on $[-\pi, \pi)$, such that

$$\int Q_{al}(f) \Psi(\theta) d\theta = 0 \quad \forall f.$$

This would allow to remove the term of order one from (A.11) and thereby yield three macroscopic equations that describe the three "constants" that characterize the equilibria defined in (A.14). However, the operator Q_{al} has only one CI ($\Psi \equiv 1$, which represents mass conservation). This necessitates the use of Generalized Collision Invariants (GCIs). Given an angle of lines $\bar{\theta}$ a GCI associated with $\bar{\theta}$ is a function $\Psi_{\bar{\theta}}(\theta)$ defined on $[-\pi, \pi)$, such that

$$\int Q_{al}(f) \Psi_{\bar{\theta}}(\theta) d\theta = 0 \quad \forall f \quad \text{with} \quad \bar{\theta}_f = \bar{\theta},$$

which is a more general concept than CIs. If three GCIs can be found, Step (ii) of the derivation now requires integrating equation (A.11) against the three GCIs associated to $\bar{\theta}_{f^\varepsilon}$. Similar to the classical, CI based approach, this removes the order one term and allows to derive the macroscopic equations. Regarding the precise functional analytical setting we refer to [20] and simply use the result therein that explicitly describes the GCIs of Q_{al} .

Lemma A.2 *Given an angle of lines $\bar{\theta}$, the space of GCIs of Q_{al} associated with $\bar{\theta}$ is*

spanned by $\chi_{\bar{\theta}}^{\pm}(\theta) := \chi^{\pm}(\theta - \bar{\theta})$ and $g_{\bar{\theta}}(\theta) := g(\theta - \bar{\theta})$ where

$$\chi^{\pm}(\theta) = \begin{cases} 1 & \text{for } \pm \cos(\theta) > 0 \\ 0 & \text{elsewhere} \end{cases}$$

and

$$g(\theta) = - \int_0^{\theta} \frac{\int_{\beta}^{\pi/2} \sin 2\alpha \exp\left(-\frac{1}{d \cos \alpha}\right) d\alpha}{\cos^2 \beta \exp\left(\frac{1}{d \cos \beta}\right)} d\beta \quad \text{for } \theta \in [0, \pi/2]$$

which is extended to $[-\pi, \pi]$ by $g(-\theta) = -g(\theta)$ and $g(\pi - \theta) = -g(\theta)$.

Note that $\chi_{\bar{\theta}}^{+}(\theta) + \chi_{\bar{\theta}}^{-}(\theta) \equiv 1$ and we recover the CI associated with mass conservation. Now we proceed as explained, by integrating (A.11) against the three GCIs associated to $\bar{\theta}_{f^{\varepsilon}}$. We only note that the main difference to [20] is the age variable s . However since Q_{al} and its properties are unaffected by s , the derivation remains largely the same. We introduce the two age-dependent density functions ρ_{\pm} as

$$\rho_{\pm}(x, s, t) = \int_{\pm(\cos(\theta - \bar{\theta}_f)) > 0} f(x, \theta, s, t) d\theta.$$

They are linked with their corresponding local mass functions by:

$$\sigma_{\pm}(x, t) = \int_0^{\infty} \rho_{\pm}(x, s, t) ds.$$

Proceeding similar to [20] finally yields

Proposition A.3 *Taking the (formal) limit $\varepsilon \rightarrow 0$ in (A.11) we obtain*

$$f^{\varepsilon}(x, \theta, s, t) \longrightarrow \bar{f}_{\rho_{+}(x, s, t), \rho_{-}(x, s, t), \bar{\theta}(x, t)}(\theta),$$

where $\bar{f}_{\rho_{+}(x, s, t), \rho_{-}(x, s, t), \bar{\theta}(x, t)}(\theta)$ is given by (A.14) and the macroscopic quantities $\rho_{\pm}(x, s, t)$ and $\bar{\theta}(x, t)$ have values in $[0, \infty)$ and $[0, \pi)$ respectively and fulfill

$$\partial_t \rho_{+} + d_1 \nabla_x \cdot (\rho_{+} v(\bar{\theta})) + \frac{1}{T} \partial_s \rho_{+} = -\Lambda(\sigma_{-}, s) \rho_{+}, \quad (\text{A.15a})$$

$$\partial_t \rho_{-} - d_1 \nabla_x \cdot (\rho_{-} v(\bar{\theta})) + \frac{1}{T} \partial_s \rho_{-} = -\Lambda(\sigma_{+}, s) \rho_{-}, \quad (\text{A.15b})$$

$$(\sigma_{+} + \sigma_{-}) \partial_t \bar{\theta} + d_2 (\sigma_{+} - \sigma_{-}) (v(\bar{\theta}) \cdot \nabla_x) \bar{\theta} + \mu v(\bar{\theta})^{\perp} \nabla_x (\sigma_{+} - \sigma_{-}) = 0, \quad (\text{A.15c})$$

supplemented by the boundary conditions

$$\rho_{+}(x, 0, t) = T \int_0^{\infty} \Lambda(\sigma_{+}, s) \rho_{-} ds, \quad \rho_{-}(x, 0, t) = T \int_0^{\infty} \Lambda(\sigma_{-}, s) \rho_{+} ds,$$

where the coefficients d_1 , d_2 and μ are given by

$$d_1 = \langle \cos \rangle_M, \quad d_2 = \frac{\langle g \frac{\sin}{\cos} \rangle_M}{\langle g \frac{\sin}{\cos^2} \rangle_M}, \quad \mu = d \frac{\langle g \sin \rangle_M}{\langle g \frac{\sin}{\cos^2} \rangle_M}, \quad (\text{A.16})$$

and $\langle \phi \rangle_M$ represents the average with respect to $M(\theta) = M_0(\theta)$:

$$\langle \phi \rangle_M = 2 \int_0^{\frac{\pi}{2}} \phi(\theta) M(\theta) d\theta = \frac{\int_0^{\frac{\pi}{2}} \phi(\theta) e^{-\frac{1}{d \cos \theta}} d\theta}{\int_0^{\frac{\pi}{2}} e^{-\frac{1}{d \cos \theta}} d\theta}.$$

Finally we remove the non-dimensionalization and revert system (A.15) back to physical units yielding (2.3)-(2.4).

A.2 Derivation of the 2-age model (2.5)

An age-discretized macro-model with $K+1$ age groups. As a starting point we use the system of equations (2.3) together with the boundary conditions (2.4), i.e. the macroscopic myxobacteria model with a continuous age variable. To derive the corresponding discrete age system we discretize the age variable s by $s_k = k\Delta s$ for $k = 0, \dots, K$, yielding $K+1$ age groups defined by

$$\tilde{\rho}_{\pm}^k(x, t) := \rho_{\pm}(x, s_k, t), \quad k = 0, \dots, K.$$

To get equations for $\tilde{\rho}_{\pm}^k(x, t)$ we use a forward difference discretization of $\partial_s \rho_{\pm}$. Since the equation for $\bar{\theta}$ is independent of s , we only need to consider the two density equations. The only noteworthy point is that the largest age group i.e. $\tilde{\rho}_{\pm}^K$ can lose particles only by reversing, not by aging. The corresponding system for a discrete age system with $K+1$ age groups is

$$\begin{aligned} \partial_s \tilde{\rho}_+^k + d_1 v_0 \nabla_x \cdot (\tilde{\rho}_+^k v(\bar{\theta})) + \frac{1}{T\Delta s} (\tilde{\rho}_+^k - \tilde{\rho}_+^{k-1}) &= -\lambda(\tilde{\sigma}_-) \phi(s_k) \tilde{\rho}_+^k, \quad \text{for } k = 0, \dots, K-1, \\ \partial_s \tilde{\rho}_+^K + d_1 v_0 \nabla_x \cdot (\tilde{\rho}_+^K v(\bar{\theta})) - \frac{1}{T\Delta s} \tilde{\rho}_+^{K-1} &= -\lambda(\tilde{\sigma}_-) \phi(s_K) \tilde{\rho}_+^K, \quad \text{for } k = K \end{aligned} \quad (\text{A.17})$$

(and analogously for $\tilde{\rho}_-^k$). The boundary conditions are included by using “virtual” age groups defined by discretizing the integrals in (2.4), yielding

$$\tilde{\rho}_+^{-1} := T\Delta s \lambda(\tilde{\sigma}_+) \sum_{k=0}^K \tilde{\rho}_+^k \phi(s_k), \quad \tilde{\rho}_-^{-1} := T\Delta s \lambda(\tilde{\sigma}_-) \sum_{k=0}^K \tilde{\rho}_+^k \phi(s_k).$$

The total group densities $\tilde{\sigma}_{\pm}(x, t)$ are defined by

$$\tilde{\sigma}_+ = \Delta s \sum_{k=0}^K \tilde{\rho}_+^k, \quad \tilde{\sigma}_- = \Delta s \sum_{k=0}^K \tilde{\rho}_-^k.$$

The 2-age macro-model. To obtain the 2-age model (2.5), we define

$$\rho_{\pm}^0(x, t) := \Delta s \tilde{\rho}_{\pm}^0(x, t), \quad \rho_{\pm}^1(x, t) := \Delta s \sum_{k=1}^K \tilde{\rho}_{\pm}^k(x, t)$$

in (A.17) and assume that $\phi(s_0) = 0$ and $\phi(s_k) = 1$ for $k \geq 1$. This yields a closed system for $(\rho_{\pm}^0, \rho_{\pm}^1)$:

$$\begin{aligned} \partial_t \rho_+^0 + d_1 v_0 \nabla_x \cdot (\rho_+^0 v(\bar{\theta})) &= -\frac{1}{T\Delta s} \rho_+^0 + \lambda(\sigma_+) \rho_-^1, \\ \partial_t \rho_+^1 + d_1 v_0 \nabla_x \cdot (\rho_+^1 v(\bar{\theta})) &= \frac{1}{T\Delta s} \rho_+^0 - \lambda(\sigma_-) \rho_+^1, \\ \partial_t \rho_-^0 - d_1 v_0 \nabla_x \cdot (\rho_-^0 v(\bar{\theta})) &= -\frac{1}{T\Delta s} \rho_-^0 + \lambda(\sigma_-) \rho_+^1, \\ \partial_t \rho_-^1 - d_1 v_0 \nabla_x \cdot (\rho_-^1 v(\bar{\theta})) &= \frac{1}{T\Delta s} \rho_-^0 - \lambda(\sigma_+) \rho_-^1. \end{aligned}$$

Name	Meaning	Value	Comment
v_0	bacterial speed	$8.8 \mu\text{m}/\text{min}$	[50]
λ_m	spontaneous reversal rate	$0.09/\text{min}$	[50, 53, 57]
λ_M	maximal reversal rate	$1.5/\text{min}$	[50, 53, 57]
$\bar{\rho}$	inflection density	$0.195/\mu\text{m}^2$	fitting parameter
T	refractory period	1 min	estimates in [31, 7]
D	angular diffusion constant	$0.1/\text{min}$	} leads to $d_1 = 0.99$
ν	alignment frequency	$100/\text{min}$	
$2m_0$	total average density	$0.25/\mu\text{m}^2$	[53]

Table 1: Biological Parameters

Name	Meaning	Value
Simulation parameters of IBM		
L_x, L_y	width and length of simulation domain	$L_x = L_y = 500\mu\text{m}$
N	total number of bacteria	$2m_0 L_x L_y = 62500$
Δt	time step	0.01 min
R	interaction radius	$5\mu\text{m}$
Simulation parameters of 1D 2-age model		
L	simulation domain	$500\mu\text{m}$
Δx	spacial step	$0.625\mu\text{m}$
Δt	time step for transport operator	$\Delta x/(2d_1 v_0) = 0.035 \text{ min}$

Table 2: Numerical Parameters

Setting $\Delta s = 1$ we get system (2.5). In Sec. 3 we demonstrate that this 2-age model is a good approximation of the full age-dependent dynamics and sufficient to reproduce and explain almost all experimentally observed features of myxobacteria.

A.3 Numerical Methods

Particle Model. The IBM of Sec. 2.1 was simulated in a square domain with periodic boundary conditions, using the circle method described in [44].

2-Age Model. We simulated the 2-age model (2.5) in one space dimension with periodic boundary conditions and $\bar{\theta} \equiv 0$. The transport and reaction terms were implemented using operator splitting with explicit upwind or downwind (for the $+$ and $-$ family respectively) finite differences for the transport term and the reaction term by an explicit Runge-Kutta (4,5) formula using the ode45 solver of Matlab.

Tab. 2 shows the parameters used for both simulation set-ups.